Severe left main coronary stenosis and mitral regurgitation in a young female patient without cardiovascular risk factors 14 years after mediastinal radiation therapy

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CLINICAL CORRESPONDENCE

Severe left main coronary stenosis and mitral regurgitation in a young female patient without cardiovascular risk factors 14 years after mediastinal radiation therapy

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A 29-year-old female with a medical history of mediastinal radiation therapy for B-cell non-Hodgkin lymphoma 14 years ago (total irradiation dose: 36 Gy) was admitted to our hospital with symptoms of chest pain and dyspnoea. Echocardiography showed a thickening of the mitral valve with a medium to severe regurgitation. A myocardial perfusion scintigraphy demonstrated anterior wall ischemia (Fig. 1) and a cardiac computer tomography scan demonstrated a non-calcified stenosis in the left main bifurcation with an approximately 50% luminal narrowing and a 70–90% non-calcified ostial stenosis in the left anterior descending artery. Coronary angiography was performed and demonstrated a significant distal bifurcation stenosis of the left main coronary artery (70%), a 90% ostial stenosis of the left circumflex coronary artery and an ostial stenosis of the left anterior descending artery (Fig. 2a, b). There was no evidence for atherosclerotic disease in other vascular regions in this patient. The patient had no cardiovascular risk factors. Laboratory studies showed total cholesterol of 4.4 mmol/l, HDL cholesterol of 1.4 mmol/l, and LDL cholesterol of 4.1 mmol/l. Erythrocyte sedimentation rate (ESR) and C-reactive protein were within the normal range. Results of serologic antibody studies for systemic lupus erythematosus or systemic vasculitis were unremarkable. Therefore, late radiation-induced coronary and valvular heart disease was considered as the most likely diagnosis. The patient underwent coronary artery bypass grafting using both internal thoracic arteries and mitral valve repair was performed. The postoperative course was uneventful.

Of note, left main stenosis in young patients in which classical risk factors of atherosclerosis are lacking may be attributed to several other causes, such as being secondary to vasculitis syndromes (Takayasu arteritis; Kawasaki syndrome). Coronary arterial involvement in Takayasu's arteritis has been described with a low incidence, i.e. approximately 10% of cases [6]. However, in particular the lack of inflammatory activation (as indicated by normal CRP and ESR) or symptoms such as fever suggested to us that coronary artery involvement of a Takayasu arteritis is not a very likely diagnosis in this patient. The lack of signs of inflammatory activity or aneurysmatic lesions of the coronary arteries argued against the Kawasaki syndrome as a likely diagnosis in this patient that does occur almost exclusively in children.

Because this patient had no laboratory signs and no clinical symptoms of inflammatory activation or manifestations nor other angiographic abnormalities, and given the known history of Hodgkin lymphoma and mediastinal radiation therapy, a postmediastinal radiation-induced coronary artery disease is highly suggestive.

Notably, exposure of the heart to ionizing radiation is considered to be associated with an increased risk of developing coronary artery and valvular heart disease, that may occur 3 up to 30 years after radiation therapy [3, 4]. A common localization of coronary lesions after radiotherapy is at the ostial or proximal segment, with a distal disease-free vasculature [8]. Aortic valve stenosis and left-sided valvular regurgitation have been most frequently associated

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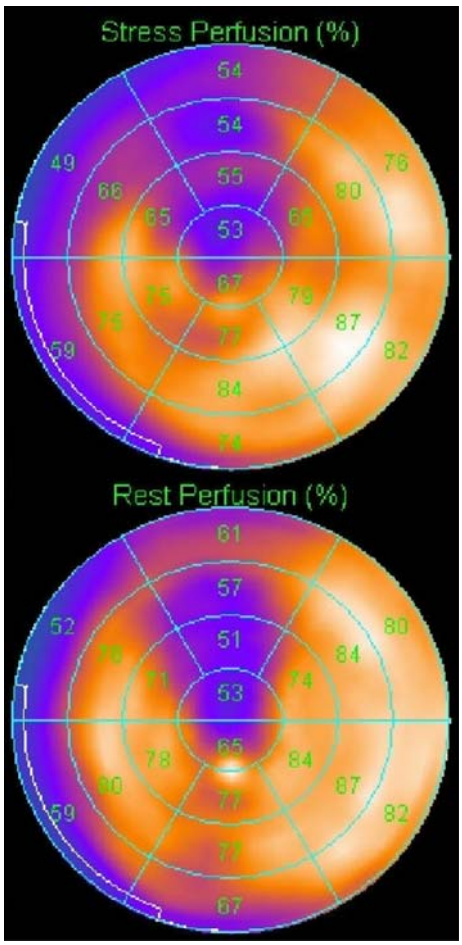

Fig. 1 Tc-99m MIBI myocardial perfusion SPECT study with bully eye images at rest and at peak stress revealed a perfusion defect of the anterior wall

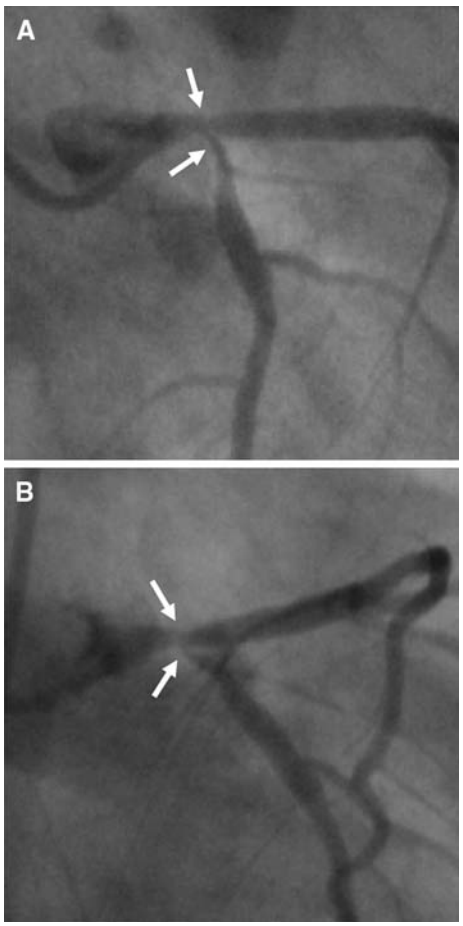

Fig. 2 Coronary angiography, showing distal bifurcation stenosis of the left main coronary artery (70%), and an ostial stenosis of the left circumflex coronary artery (90%)

with radiation therapy [4, 5]. Coronary bypass grafting is frequently performed in these patients given recent observations of an unacceptably high rate of restenosis after coronary stenting in excess of 80% at least with the use of bare metal stents [10]. There are no studies or case reports available at present about the impact of drug-eluting stents on coronary restenosis in patients with radiation-induced coronary disease. However, one would assume that the results might be more favorable. In our patient, given the anatomy and location of coronary stenoses and accompanying valvular heart disease, we did not consider coronary stenting as an optimal revascularization strategy. Notably, there has been concern regarding potential radiation damage to the internal thoracic arteries [9]. A recent registry from the Mayo Clinic, however, suggests a better outcome in patients after mediastinal radiation therapy receiving internal thoracic artery grafts rather than venous bypass grafting [1]. Overall, the outcome of coronary bypass surgery may be less favorable in patients after mediastinal radiation [1], and a close follow-up should be recommended.

It is estimated that 5.5–12% of patients receiving mediastinal radiation develop radiation-induced coronary artery disease with a latency of onset of 3–30 years [7]. Although the pathogenesis of radiation-induced coronary artery disease is complex and not fully understood, it is associated with marked adventitial fibrosis and thickening, medial thinning and destruction and a greater calcium and lipid content within intimal plaques [11]. It is suggestive that leaflets of valves may undergo fibrotic changes with or without calcification [2]. However, the exact pathogenesis of radiation-induced coronary disease has not been studied in detail. At present, this will intensely examined in the CARDIORISK project, an integrated database funded by the European Commission in the 7th Framework Program (http://www.cardiorisk.eu/index.php) that will hopefully lead to novel approaches to prevent this important late complication of mediastinal radiotherapy.

This report suggests that doctors should be highly alert for symptoms of coronary disease that can be very severe, even in young female patients after radiation therapy.

Based on current data, a long-term follow-up for early detection of coronary or valvular heart disease needs to be considered in patients after mediastinal radiotherapy.

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